

A Case of Chromomycosis Treated by Surgical Therapy Combined with Preceded Oral Administration of Terbinafine to Reduce the Size of the Lesion

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(Received May 27, 2011; Accepted November 4, 2011)

Chromomycosis is a chronic fungal disease of the skin and subcutaneous tissues caused by a group of dematiaceous black fungi [1]. Small lesions can be removed with excision, but other cases are difficult to treat. We report a case of chromomycosis caused by *Fonsecaea pedrosoi* (*F. pedrosoi*). The case involved a 74-year-old man, who had noted a lesion on the back of the right thigh, that was gradually enlarging and reaching up to 30 cm in diameter, in 20-years. From microscopic examination, sclerotic cells were seen. We diagnosed this case as chromomycosis caused by *F. pedrosoi* on mycological examination. The patient was initially treated with oral terbinafine (250mg/day) as the lesion was very large. After the 18 months treatment, the size of the lesion reduced to 1cm, then the remaining lesion was excised.

Key words: chromomycosis, *Fonsecaea pedrosoi*, terbinafine, surgery

INTRODUCTION

Chromomycosis is a term applied to infection with some black dematiaceous fungi and is characterized by sclerotic pigmented bodies intermediate between a yeast and hyphal form in the tissues. Infections have occurred throughout the world. The fungi are thought to be present in soil, wood and vegetable debris. Chromomycosis is particularly seen in farmers and agricultural workers, because the infection occurs primarily in skin following trauma [2]. Chromomycosis is treated with surgery, antifungal agents or local thermotherapy. The preferred treatment of small and localized lesions is usually surgical excision with wide surgical margins to prevent local recurrence. However, surgical treatment is often not feasible for deep lesions or for those with extensive cutaneous involvement. For deep or extensive lesions, prolonged treatment with systemic antifungal agents alone or in combination provides the best chance of cure [1].

Here, we report a case of a chromomycosis with a large lesion, which were treated by oral terbinafine to reduce size and subsequently excised.

CASE REPORT

A 74-year-old fisherman presented with a 20-year history of a slowly enlarging lesion on the back of his right thigh. It had been diagnosed as tinea corporis by local dermatologists and treated with topical ketoconazole and terbinafine. However, the eruption had

enlarged despite treatment, and he was referred to our hospital.

On clinical finding, there was an annular erythema approximately 30 × 30 cm in size. The border of the ring was 2 cm in width, slightly rose, discontinuous and accompanied with scales on the surface (Fig. 1a). The scales showed sclerotic cells in direct mycological exams with 10% KOH (Fig. 2a). Laboratory data were all within normal limits except for positive HCV antibody. There were no significant findings on the abdominal ultrasonography, and computed tomography showed an old cerebral infarction.

The skin biopsy was carried out on the edge of the erythema. The histological finding was showed acanthosis, epithelioid cell granuloma including multinucleated giant cells, and neutrophilic infiltration in the dermis (Fig. 3a). Sclerotic cells were recognized on PAS staining (Fig. 3b). Examination of the mycological culture on Sabouraud's dextrose agar at room temperature showed growths of heaped and fuzzy colonies with black surface (Fig. 2b). Slide culture showed the fungal morphology to be of the *Rhinocladiella*-type (Fig. 2c). The ITS-RFLP pattern matched for *Fonsecaea pedrosoi* (rDNA type 2) [3]. The diagnosis of chromomycosis was made at by mycological evaluation that confirmed the presence of fungal cells, identified in the following culture as *Fonsecaea pedrosoi* (*F. pedrosoi*).

Treatment with terbinafine of 250mg/day was started. In 10 weeks, the lesion began to disappear partially. 18 months after the initiation of terbinafine, there was



Fig. 1 Clinical features (on the back of patient's right thigh)

- a First examination
An annular erythema approximately 30 × 30 cm in size. The border of the ring was 2 cm in width, slightly rose, discontinuous and accompanied with scales on the surface.
- b 18 months after treatment
Pigmentation and 3 erythematous lesions, each of 1 cm in size, with scaly surface.
- c 3 months after surgical excision
Postoperative lesion showing no sign of recurrence.

a good clinical response, with mostly pigmentation left and three erythematous lesions 1-cm in diameter on the edge of the original lesion (Fig. 1b). At this point, scales did not show sclerotic cells in direct mycological examination with 10% KOH. Treatment with terbinafine was continued for a total of 32 months, but there was little clinical improvement (the period of terbinafine treatment is not exactly accurate as the medication was interrupted during a hospital admission for a bone fracture and he had been non-compliant at this period). The remaining lesions we excised with a 5 mm margin. When the excised specimen was cultured, *F. pedrosoi* was negative in the pigmented lesion and positive in the erythematous lesion. There was no clinical recurrence three months after surgical excision (Fig. 1c).

DISCUSSION

Chromomycosis is a subcutaneous mycosis caused by the dematiaceous fungi *Fonsecaea*, *Phialophora* and *Cladophialophora* [4]. It is seen worldwide, but is most commonly seen in tropical and subtropical regions [1]. In Japan, it has been reported that *F. pedrosoi* is the most common causative fungus, accounting for 87%

of the disease in this country [5]. It starts as a scaly papule, often following superficial trauma, which slowly expands into a verrucous nodule or plaque [6]. The course of the infection is chronic, slowly progressive, and it is often asymptomatic [4].

An Ichushi-Web database (Japan Medical Abstracts Society, JAMAS, <http://www.jamas.or.jp/>) search was conducted using the key word “chromomycosis” for papers published from 1997 to 2009 in Japan. As a result, there have been 64 reports, including our case, and a total of 35 cases (54.6%) were caused by *F. pedrosoi*. From the 35 cases [5, 7–35, 37–39] that was caused by *F. pedrosoi*, the male to female ratio of these cases were 1 to 0.94. The age of patients ranged from 36 to 89 years of age with the greatest number of patients in the 60–69 years age group. Lesions were most commonly found on the arms (40%).

Oral antifungal agents for chromomycosis include fluconazole, flucytosine, ketoconazole, terbinafine and itraconazole. In the 1990's, terbinafine and itraconazole were the most popular agents. The reported response rate of these agents in chromomycosis was 60% for itraconazole and 66.7% for terbinafine [36]. As patient in this case was on many other medications

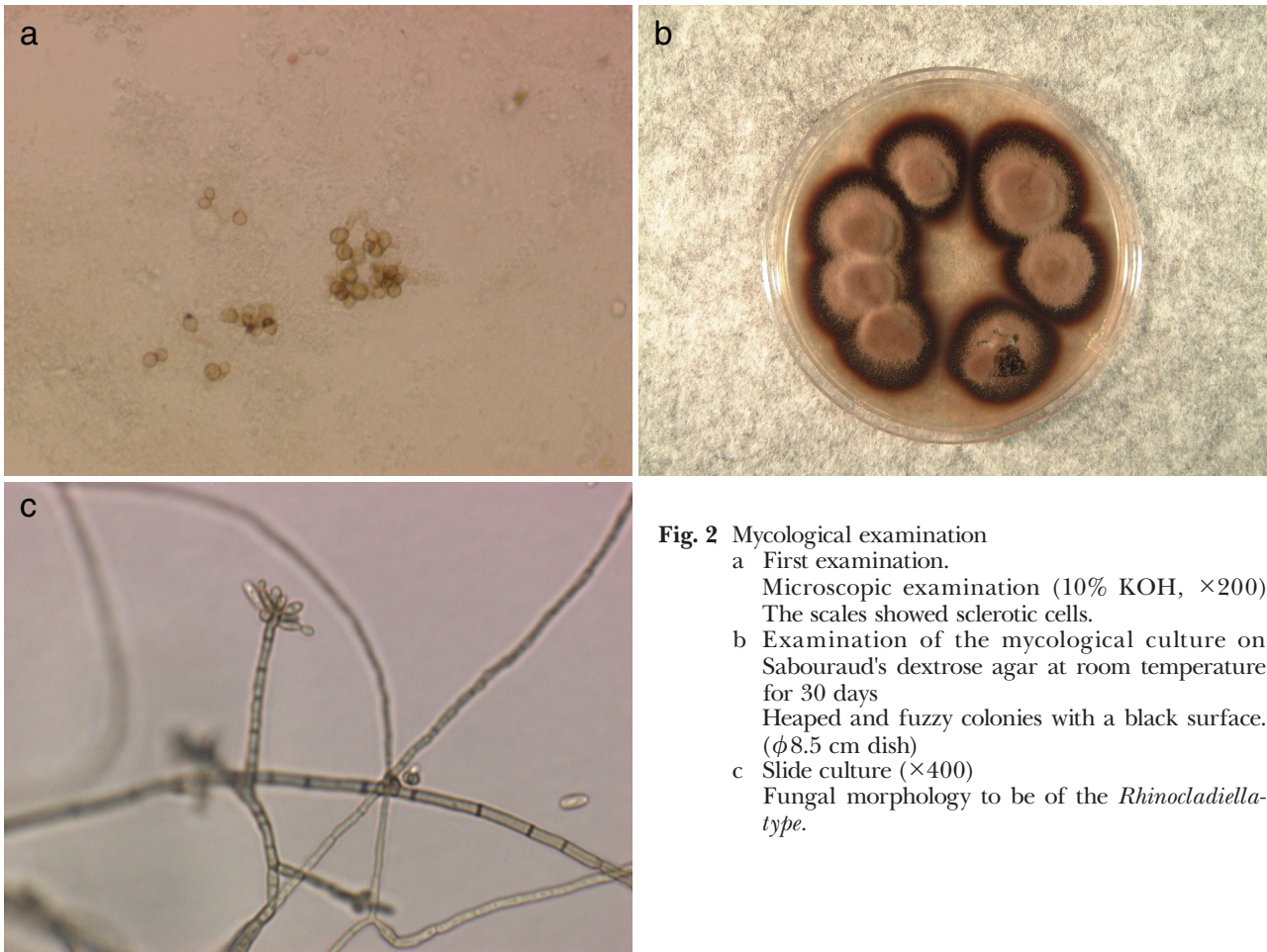


Fig. 2 Mycological examination

- a First examination.
Microscopic examination (10% KOH, $\times 200$)
The scales showed sclerotic cells.
- b Examination of the mycological culture on Sabouraud's dextrose agar at room temperature for 30 days
Heaped and fuzzy colonies with a black surface. ($\phi 8.5$ cm dish)
- c Slide culture ($\times 400$)
Fungal morphology to be of the *Rhinocladiella*-type.

for hepatitis C, cerebral infarction, hypertension; ICTZ was not selected to avoid potential interaction with Ca-blocker for hypertension. 1997 was the year when terbinafine became available in Japan. Since 1997, 17 reported cases of chromomycosis have been treated with terbinafine, of which 9 cases were caused by *F. pedrosoi*. Many reported cases did not respond to terbinafine 125mg/day, prompting either a dose increase to 250mg/day, a change in medication, surgical removal or addition of local thermotherapy [5, 36].

Local thermotherapy has few side effects but requires prolonged treatment and perseverance of patients [37]. We did not use local thermotherapy because the patient refused this treatment.

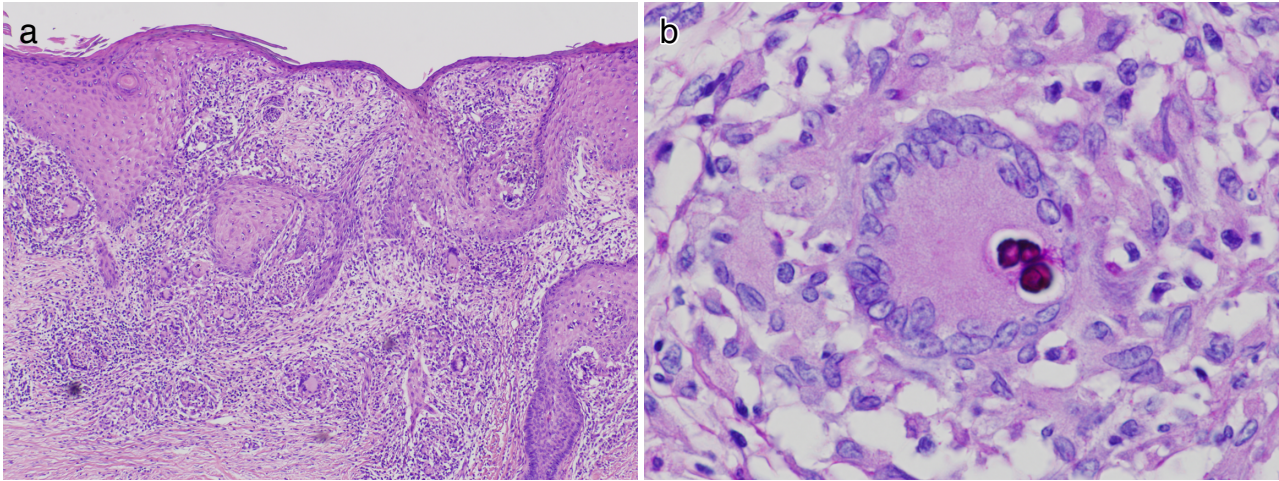
Surgical removal of lesions is considered the most preferred treatment [38]. It is difficult to surgically remove large lesions due to the possibility of scarring. If the lesion is small and localized, we can excise the lesion with a 5 mm margin [36]. The maximum excised area in past reports was 3.7×3.5 cm in size [39]. At the initial presentation of our case, the lesion was 30 cm in size and thus, the operative risk was high. Terbinafine at 250mg/day orally was considered to be the treatment of choice compared with surgical resection, local thermotherapy and itraconazole. As there was little clinical improvement after 32 months of terbinafine administration, we excised the remaining lesion and there has been no evidence of recurrence to date.

There have been 35 cases of chromomycosis caused by *F. pedrosoi*, reported in Japan from 1997 to 2009.

Among 35 reports, 15 cases has been managed surgically, 8 cases treated with only antifungal agent, 6 cases treated by combination of antifungal agent and local thermotherapy, 2 cases is other treatments and 4 cases are unknown. 11 cases among the surgically removed 15 cases have showed no recurrence (Table 1). However, only one case out of the orally treated 8 cases has been treated successfully.

Chromomycosis recur easily, and is often intractable. We stopped oral terbinafine 3 weeks after the surgery because culture of the excised pigmented lesion was negative. There was no recurrence three months after surgical excision. Oral administration of terbinafine 250mg/day could reduce in size, however, it could not completely cure [5, 36, 38]. Monotherapy with orally administered antifungal agent may not lead to a complete cure. Combination therapy should be considered taking into account the state of the lesion. Our case report demonstrated that in the case of large lesions, oral terbinafine may be administered first to reduce the size of the lesions prior to surgical removal.

(This report was presented at the 25th Annual Meeting of Japan Organization of Clinical Dermatologists)

**Fig. 3** Histological features

- a Acanthosis, epithelioid cell granuloma including multinucleated giant cells and neutrophilic infiltration in the dermis. (H-E staining, $\times 40$)
 b Sclerotic cells are found within giant cells. (PAS staining, $\times 400$)

Table 1 Summary of Japanese cases of chromomycosis caused by *F. pedrosoi* which were surgically removed.

Patient No.	Age	Sex	Site of Lesion	Size	Preoperation	Postoperation	Effect	Reference No.
1	71	M	knee	2.1 $\times$ 2.5 cm	ND	antifungal agents	no recurrence	11
2	69	M	buttock	13 cm	antifungal agents local thermotherapy	antifungal agents local thermotherapy	—	12
3	62	M	foot	—	antifungal agents local thermotherapy	ND	no recurrence	13
4	71	F	cheek	—	ND	antifungal agents	recurrence	14
5	68	F	waist	6 cm	antifungal agents local thermotherapy	ND	—	15
6	62	F	hand	2.5 $\times$ 1.7 cm	antifungal agents	ND	no recurrence	16
7	59	M	back	3.0 $\times$ 3.5 cm	local thermotherapy	antifungal agents	—	17
8	87	F	cheek	1.1 $\times$ 0.8 cm	—	—	no recurrence	18
9	60	M	arm	1 cm	—	—	no recurrence	19
10	62	F	foot	3.6 $\times$ 2.5 cm	—	antifungal agents	no recurrence	20
11	36	M	arm	2.0 $\times$ 1.8 cm	—	—	no recurrence	37
12	67	F	arm	1.5 cm	—	—	no recurrence	21
13	84	F	buttock	2.0 cm	—	antifungal agents local thermotherapy	no recurrence	22
14	78	M	arm	3.7 $\times$ 3.5 cm	antifungal agents local thermotherapy	antifungal agents	no recurrence	39
15	74	M	thigh	30 $\times$ 30 cm	antifungal agents	antifungal agents	no recurrence	this case

Not done: ND

Not mentioned: —

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